UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

KD

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/972,301	11/18/97	COLEMAN T	325800-588(P

HM12/0911

MICHELLE S. MARKS
HUMAN GENOME SCIENCES, INC.
9410 KEY WEST AVENUE
ROCKVILLE MD 20850

EXAMINER	
KEMMERER, E	
ART UNIT	**PAPER NUMBER**
1646	21

DATE MAILED: 09/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/972,301	Coleman et al.
Examiner	**Group Art Unit**
Elizabeth C. Kemmerer	1646

☒ Responsive to communication(s) filed on *6 Jul 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *90-136* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *90-136* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____ .

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Status of Application, Amendments, And/Or Claims

The amendment filed 06 July 2000 (Paper No. 20) has been entered in full. Claims 1-89 are canceled. Claims 90-136 are pending and under examination.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claims 89 under 35 U.S.C. § 102(b) as set forth at p. 7 of the previous Office Action (Paper No. 16, 07 January 2000) is *withdrawn* in view of the canceled and newly presented claims (Paper No. 20, 06 July 2000).

35 U.S.C. § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 90-136 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Claims 90-136 are directed to EMAP III polypeptides. The specification discloses EMAP III which has the structure of 1-168 of SEQ ID NO: 2 or is encoded by the deposited human cDNA clone. EMAP III

shares significant sequence identity with a polypeptide known as EMAP II. Based on this sequence identity, the specification speculates that EMAP III has similar biological activities to EMAP II. No biological activities have been specifically demonstrated for EMAP III. The assertion that EMAP III has similar biological activities as EMAP II cannot be accepted in the absence of supporting evidence, because the relevant literature reports examples of closely related polypeptides belonging to a polypeptide family wherein individual members have distinct, and sometimes even opposite, biological activities. For example, Vukicevic et al. (1996, PNAS USA 93:9021-9026) disclose that OP-1, a member of the TGF-β family of proteins, has the ability to induce metanephrogenesis, whereas closely related TGF-β family members BMP-2 and TGF-β1 had no effect on metanephrogenesis under identical conditions (p. 9023, paragraph bridging columns 1-2). Similarly, PTH and PTHrP are two structurally closely related proteins which can have opposite effects on bone resorption (Pilbeam et al., 1993, Bone 14:717-720; see p. 717, second paragraph of Introduction). Identifying the biological activities of EMAP III would require substantial research. Basic research, such as studying the properties of the claimed product or the mechanisms in which the product is involved, does not constitute a substantial utility. Thus, the specification fails to support a specific and substantial utility for EMAP III and variants and fusion proteins thereof. Furthermore, the specification does not support any other specific and substantial utility for the disclosed EMAP III involving features unrelated to the asserted biological activity. For example, there is no disclosure of particular disease states correlating to an alteration in levels or forms of EMAP III such that EMAP III could be used

as a diagnostic tool. Therefore, the skilled artisan is not provided with sufficient guidance to use the claimed polypeptides for any specific and substantial utility.

35 U.S.C. § 112, First Paragraph

Claims 90-136 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation.

Furthermore, the claims encompass polypeptide variants of the polypeptide of SEQ ID NO: 2, i.e. substitutions, deletions or insertions in a protein corresponding to SEQ ID NO: 2; should Applicant establish a specific and substantial utility for the claimed polynucleotides, Applicant has not provided sufficient guidance as to how to make and use the encoded polypeptides which are not 100% identical to the polypeptide of SEQ ID NO: 2, but which still retain a desired property of the polypeptide of SEQ ID NO: 2.

The specification has failed to teach one of skill in the art which amino acid substitutions, deletions or insertions to make. Furthermore, the Applicant has not provided guidance as to what properties of the allelic variants or sequence variants of the protein corresponding to SEQ ID NO: 2 might be desired nor any guidance as to which amino acid substitutions, deletions or insertions to

make to achieve any desired property. The problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. While it is known that many amino acid substitutions are generally possible in any given protein, the positions within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of success are limited. Certain positions in the sequence are critical to the protein's structure/function relationship, e.g. such as various sites or regions directly involved in binding, activity and in providing the correct three-dimensional spatial orientation of binding and active sites. These or other regions may also be critical determinants of antigenicity. These regions can tolerate only relatively conservative substitutions or no substitutions (see Bowie et al., 1990, Science 247:1306-1310, especially p.1306, column 2, paragraph 2; Wells, 1990, Biochemistry 29:8509-8517; Ngo et al., 1994, The Protein Folding Problem and Tertiary Structure, pp. 14-16). However, Applicant has provided little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (e.g. such as by amino acid substitutions or deletions), and the nature and extent of changes that can be made in these positions. Although the specification outlines art-recognized procedures for producing and screening for active muteins, this is not adequate guidance as to the nature of active analogs that may be constructed, but is merely an invitation to the artisan to use the current invention as a starting point for further experimentation. Even if an active or binding site were identified in the specification, they may not be sufficient, as the ordinary artisan would immediately recognize that an active or binding site must

assume the proper three-dimensional configuration to be active, which conformation is dependent upon surrounding residues; therefore substitution of non-essential residues can often destroy activity.

Due to the large quantity of experimentation necessary to determine an activity or property of EMAP III such that it can be determined how to use EMAP III, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art establishing that biological activity cannot b predicted based on structural similarity, and the breadth of the claims which fail to recite particular biological activities and also embrace a broad class of structural fragments and variants, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Applicant's arguments (pp. 9-11, Paper No. 20, 06 July 2000) have been fully considered but are not deemed to be persuasive for the following reasons.

Applicant asserts that the Examiner has provided no reasonable basis to doubt the objective truth or accuracy of the disclosure. Applicant states that the Examiner has found only a few cases of proteins completely unrelated to the instantly claimed proteins wherein there is no correlation between structure and function. Applicant also urges that the Examiner has not provided reasoning why the claimed proteins cannot have the asserted utilities. Applicant reviews the specification's disclosure of the structural relationship between EMAP II and EMAP III, and the known activities of EMAP II. Applicant concludes that the Examiner's examples are not particularly relevant to EMAP II or III, and the rejection should be withdrawn. This has been fully considered but is not

found to be persuasive. The examples of proteins having structural similarity but no functional similarity cited by the examiner in the previous Office Actions are simply a few examples of the many instance in nature wherein this phenomenon occurs. The examples provide evidence that one skilled in this art would not reasonably predict a functional similarity between proteins based solely on a structural similarity. Applicant has provided no evidence of structurally related proteins more closely related to EMAP II and III wherein structural similarity can reasonably be relied upon as a predictor of functional similarity. If Applicant has such evidence, such should be submitted on the record as it would be highly probative. Similarly, if any post-filing date data have been generated regarding the predicted activities of EMAP III, such would also be highly probative.

Claims 96-105 and 123-136 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 96-105 and 123-136 contain new matter. Specifically, there is no support in the specification as filed for ATCC Deposit Number 97132. This issue had been resolved previously (e.g., see Applicant's response of 31 March 1999, Paper No. 9, p. 3) wherein Applicant agreed that there was a typographical error. "97132" should be "97165."

35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 94, 104, 111, 121 and 135 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The preambles of these claims are directed to a composition, whereas the remainder of the claims is directed to a single compound (protein). Therefore, it is unclear whether the metes and bounds of the claim embrace compounds only or compositions. Amending the claims to recite "and a carrier" would be remedial.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth C. Kemmerer, Ph.D., whose telephone number is (703) 308-2673. The examiner can normally be reached on Mondays through Thursdays from 6:30 a.m. to 4:00 p.m. The examiner can also normally be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler, Ph.D., can be reached on (703) 308-6564.

Official papers filed by fax should be directed to (703) 308-4242. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

ECK
September 7, 2000

ELIZABETH KEMMERER
PRIMARY EXAMINER